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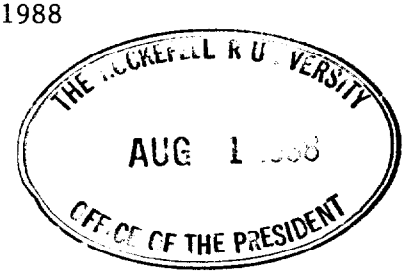

Dr. Joshua Lederberg, President
The Rockefeller University
New York, NY 10021

Dear Dr. Lederberg:

Thank you for your note regarding the appearance of "new" virus diseases of humans and the reprint of your January 20 lecture in Paris. I share your concerns regarding the possibility of emerging virus pandemics. It is not a question of "whether?" there will be new virus scourges challenging the expanding human population, but "when?", "what kinds of viruses?", and "how rapid and how serious the spread?". Rapid virus evolution is so dominated by stochastic events that predictability cannot even be hoped-for. Although I have studied persistent virus infections for decades, I was frankly surprised that the most recent challenge has come from the slowly-replicating, chronic, close-contact infections by AIDS viruses. I had expected (and still expect) that we are more vulnerable to newly-arisen acute RNA virus diseases with very short incubation periods; rapid, high-level virus replication; and high transmissibility by the respiratory route.

I have not written much on this perplexing topic (I enclose reprints of the Annual Reviews paper and an earlier review in Science). Esteban Domingo and I have an extensive review of RNA virus variability in Volume III ("Variability of RNA Genomes") of RNA GENETICS, C.R.C. Press, Boca Raton. This volume (1988) contains a number of reviews regarding rapid evolution of RNA viruses. The final article, "Sequence Space and Quasispecies Distribution" by Manfred Eigen and Christof Biebricher, provides an intriguing, quantitative, theoretical treatment of RNA virus evolution, fitness topography, mutation frequencies, and error thresholds, population structures, etc.

I have not thought much about possible surveillance and rapid response mechanisms. One virologist who has (at least with regard to arthropod-borne viruses) is Bob Shope at Yale. The U.S. Army Medical Research and Development Command maintains a strong interest in this problem, but I don't know what mechanisms they have at hand for surveillance.

With best wishes,

Sincerely,

John Holland

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Enclosures